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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,227	06/25/2001	Hermann Bujard	BBI-013C2CN2	7548

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/892,227	BUJARD ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-26 and 31-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-26 and 31-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Response to the First Action on the Merits was filed May 25, 2005. Claim 35 is amended.

Claims 23-26 and 31-40 are pending.

Information Disclosure Statement

The information disclosure statement filed October 15, 2002, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Applicants have indicated that a Supplemental IDS listing of each reference on the IDS filed October 15, 2002 that was not initialed by the Examiner was provided. Additionally, a copy of each reference was provided. However, no supplemental IDS was provided, nor are there any copies of the references of the supplemental IDS.

Claims

With regards to claims from a related application, 09/874,389 (Mail Room Date of January 25, 2005) being included in the PAIR Image File Wrapper, the Examiner had included them as a reference for the Double Patenting rejection.

Withdrawn Rejections

35 U.S.C. 112, First Parag., Written Description

Applicant's arguments, see Applicant's response, pages 9-10, filed, May 25, 2005 with respect to claims 23-26, 31-40, have been fully considered and are persuasive. The rejection of claims 23-26, 31-40 has been withdrawn.

New and Maintained Rejections

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 24 is provisionally rejected in modified form under 35 U.S.C. 101 as claiming the same invention as that of claims 37 and 44 of copending Application No. 09/874,389 ('389) for reasons of record, January 25, 2005. Both inventions are drawn to a transgenic non-human animal whose genome comprises a tet operator-linked gene and a transgene comprising a nucleic acid sequence encoding a fusion protein comprising a Tet repressor and a second polypeptide which directly or indirectly

activates transcription in eukaryotic cells operably linked to a transcriptional regulatory element.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-26, 31, 33-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 37, 42-44 of copending Application No. 09/874,389 ('389). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 23, 25, 31, 33, 35-39 of the instant invention are more narrow in scope than the claims of 37, 42, 43 of '389. Claims 23, 25, 31, 33, 35-39 of the instant invention and claims 37, 42, 43 of '389 are drawn to a transgenic non-human animal having integrated into the genome of the non-human animal and also having a tet operator-linked gene in the genome of the non-human animal, wherein the transgene comprises a nucleotide

sequence encoding a fusion protein which is comprised of a polypeptide that activates transcription directly or indirectly and of a Tet repressor, operably linked to a transcriptional regulatory element, and wherein the tet-operator linked gene is expressed at detectable levels. The claims are similarly drawn to the transcriptional activator comprising the transcription activation domain of herpes simplex virion protein 16. Claims 23, 25, 31, 33, 35-39 of the instant invention are more narrow in scope than claims 37, 42, 43 of '389, as the claims encompass an additional embodiments that the fusion protein binds to the tet operator in the absence of tetracycline or a tetracycline analog and that the transgenic animals are selected from the group of a mouse, a cow, a sheep, a goat, and a pig. Claims 26, 34 of the instant invention have a narrower scope than claim 44 of '389 in that the claims are drawn to embodiments of a transcription activation domain of herpes simplex virion protein 16, and that the animals are selected from the group consisting of a mouse, a cow, a sheep, a goat, and a pig. Therefore, the embodiments of the instant invention are encompassed by the '389 claims and that the specific embodiments are taught in the '389 specification such that they are obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 23-26, 31-40 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S.

Patent No. 5,859,310 ('310) for reasons of record set forth in the previous Office Actions of June 17, 2003 and January 25, 2005.

Response to Arguments

It is noted that Applicants have stated on May 25, 2005, January 8, 2004, and November 15, 2004 that upon indication that the pending claims are allowable will the terminal disclaimer be submitted.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-26, 31-40 remain rejected in modified form under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a transgenic mouse comprising a transgene comprising a nucleic acid sequence encoding luciferase operably linked to a tetracycline-responsive promoter (p_{hCMV^*-1} (SEQ ID NO.5)) integrated into the genome of the mouse and a nucleic acid sequence encoding the tetracycline-regulated transcriptional activator (tTA (SEQ ID NO. 1)) operably linked to a human CMV IE promoter (position +75 to –675 and a rabbit β-globin polyadenylation site including an intron integrated into the genome of the mouse

does not reasonably provide enablement for

the full breadth of any transgenic non-human animal comprising a transgene integrated into the genome of the animal and a tet-operator-linked gene in the genome of the animal wherein the transgene comprises a nucleic acid sequence encoding a fusion protein which activates transcription of a tet operator linked gene at a detectable level, wherein the fusion protein comprises a Tet repressor operatively linked to a polypeptide that directly or indirectly activates transcription in eukaryotic cells.

for reasons of record set forth in the Office Actions of October 3, 2002, June 17, 2003, March 15, 2004, January 25, 2005 and as discussed below. It is noted that compared with the previous Office Action, the present scope of enablement is narrower. The scope of the previous Office Actions was transgenic mice. However, now, the scope has been narrowed to the mice taught in the specification. The scope is narrower because in light of the teachings of Hammer et al., as discussed in the previous Office Actions, an artisan cannot predict what the phenotype is of a transgenic mouse comprising the tet system, wherein any heterologous protein is expressed. Because the art teaches unpredictability in phenotype exhibited by transgenic mice that overexpress heterologous proteins and the specification does not teach an artisan how to overcome the teachings of the art, an artisan would need to determine empirically whether each heterologous protein expressed in a transgenic mouse has a phenotype corresponding to the overexpression. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments, pages 7-9 of Applicant's response, filed May 25, 2005 have been fully considered but they are not persuasive.

With regards to the Applicant's argument that "enablement of the claimed invention does not require a skilled artisan to be able to make and use a transgenic animal exhibiting a phenotype (Applicant's response, page 7, part A)," the Examiner does not find the argument persuasive. The art teaches that there are many examples in which transgenic non-human animals have been made and which exhibit no phenotype (e.g. see Duff et al., 1996, Nature, 383: 710-713, who teach that mice that overexpress presenilin 1 (PS1) exhibit no phenotype). For an artisan, this means that the transgenic animal looks similar to the wild type control and cannot be used to compare differences between the wild type state of the animal and the state as a result of the transgene. The breadth of the claims, as written, encompasses transgenic non-human animals which have no phenotype. Neither the specification nor the art teaches an artisan how to use any transgenic non-human animals that exhibit no phenotype. For this reason, the specification does not enable the artisan to practice the claimed invention for its fullest breadth.

With regards to the Applicant's argument that the claimed invention encompass transgenic animals, wherein the animals lack a phenotype are usable by artisans as these animals can express a protein of interest in the milk of the animal (Applicant's argument, page 8, section B), the Examiner does not find the argument persuasive. The reason for this is because while the specification contemplated the idea on page 41

of the specification, nothing in the specification teaches an artisan what proteins could be expressed in milk, nor was any guidance provided as to how one would obtain and purify the protein of interest from the milk. The art teaches that protein purification is an empirical process. The specification does not provide any guidance as to how one would obtain any protein secreted in the milk by transgenic animals. Further, the claims are not so limited and read broadly on the expression of any protein, including intracellular and transmembrane proteins which are not capable of being secreted.

With regards to the Applicant's response that the specification provides extensive guidance of how to prepare a transgenic animal comprising a transgene, as claimed, the Examiner does not find the argument persuasive. The reason for this is because the focus of the Examiner's argument was not so much that the specification lacked the steps needed to generate a transgenic animal comprising the tet transgene system. Rather, the specification lacked guidance that teaches an artisan how to anticipate any phenotype using any transgenic non-human animal comprising the tet transgene system. This means that the specification has not taught an artisan how to anticipate all phenotypes (and lack of phenotypes) in all transgenic animals made by this system. The Examiner has pointed to the teachings of Hammer et al. who teach that not all heterologous transgenes will function similarly in all species of animal (e.g. see Office Action of October 3, 2002, pages 9-10 and Office Action June 17, 2003, page 6). The Examiner has indicated that an artisan cannot predict whether any gene of interest under the control of the tet operator will necessarily have activity (Office Action, October 3, 2002, page 9, line 5). Thus, with regards to the instant invention, nothing in the

specification teaches an artisan how to overcome the teachings in the art, wherein an artisan could predict that expression of a heterologous gene of interest will result in a phenotype in any transgenic non-human animal, such that an artisan could detect a phenotype and use the animal. It would be undue experimentation for an artisan to determine the phenotypes for each transgene in every species of animal. It would also be undue experimentation for an artisan to know what are the parameters used to determine whether a transgenic animal would exhibit a phenotype when expressing a heterologous transgene and if that animal exhibited a phenotype, what the phenotype would be, as the specification and the art do not provide any guidance.

Thus, for the reasons described above, while the specification enables an artisan to make and use a transgenic mouse comprising a transgene comprising a nucleic acid sequence encoding luciferase operably linked to a tetracycline-responsive promoter (p_{hCMV^*-1} (SEQ ID NO.5)) integrated into the genome of the mouse and a nucleic acid sequence encoding the tetracycline-regulated transcriptional activator (tTA (SEQ ID NO. 1)) operably linked to a human CMV IE promoter (position +75 to –675 and a rabbit β-globin polyadenylation site including an intron integrated into the genome of the mouse, the specification does not reasonably provide enablement commensurate with the full scope of the claims.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH

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PRIMARY EXAMINER